



US005432176A

United States Patent [19]**Walser**[11] **Patent Number:** **5,432,176**[45] **Date of Patent:** **Jul. 11, 1995**[54] **METHOD OF RETARDING THE PROGRESSION OF CHRONIC RENAL FAILURE**[75] Inventor: **Mackenzie Walser, Ruxton, Md.**[73] Assignee: **The John Hopkins University, Baltimore, Md.**[21] Appl. No.: **996,757**[22] Filed: **Dec. 24, 1992****Related U.S. Application Data**

[63] Continuation-in-part of Ser. No. 277,161, Nov. 29, 1988, Pat. No. 5,175,144.

[51] Int. Cl.⁶ **A61K 31/495; A61K 31/50; A61K 37/00; A61K 31/56**[52] U.S. Cl. **514/252; 514/2; 514/11; 514/171; 514/289; 514/327**[58] Field of Search **514/2, 11, 179, 252, 514/282, 289, 327, 171**[56] **References Cited****U.S. PATENT DOCUMENTS**

3,714,159	1/1973	Janssen et al.	424/601
4,107,306	8/1978	Voorhees	514/171
4,320,146	3/1982	Walser	424/601

FOREIGN PATENT DOCUMENTS

2116425 9/1983 United Kingdom .

OTHER PUBLICATIONS

Remington's Pharmaceutical Sciences, 16th edition, 1980, pp. 1858-1859.

M. Moguilewsky, et al., "RU 38486: Potent Anti-glucocorticoid Activity Correlated with Strong Binding to the Cytosolic Glucocorticoid Receptor Followed by an Impaired Activation", *S. Steroid Biochem*, vol. 20, No. 1, pp. 271-276 (1984).Roland M. Schaefer, et al., "Evidence for Reduced Catabolism by the Antiglucocorticoid RU 38486 in Acutely Uremic Rats", *Am. J. Nephrol*, 7, pp. 127-131 (1987).Xavier Bertagna, et al., "The New Steroid Analog RU 486 Inhibits Glucocorticoid Action in Man", *Journal of**Clinical Endocrinology and Metabolism*, vol. 59, No. 1, pp. 25-28 (1984).N. Gretz, et al., "Low-protein diet supplemented by keto acids in chronic renal failure: A prospective controlled study", *Kidney International*, vol. 24, Suppl. 16 (1983), pp. S-263-S-267.M. Walser, "Ketoacids in the treatment of uremia*", *Clinical Nephrology*, vol. 3 No. 5 (1975).G. Barsotti, et al., "Effects on Renal Function of a Low-Nitrogen Diet Supplemented with Essential Amino Acids and Ketoanalogues and of Hemodialysis and Free Protein Supply in Patients with Chronic Renal Failure", *Nephron* 27:113-117 (1981).W. E. Mitch, et al., "The Effect of Keto Acid-Amino Acid Supplement to Restricted Diet on the Progression of Chronic Renal Failure", *The New England Journal of Medicine*, 311:623-629 (Sep. 6), 1984.J. Burns, et al., "Comparison of the effects of keto acid analogues and essential amino acids on nitrogen homeostasis in uremic patients on moderately protein-restricted diets", *The American Journal of Clinical Nutrition* 31: Oct. 1978, pp. 1767-1775.M. Walser, et al., "Progression of chronic renal failure in patients given ketoacids following amino acids", *Kidney International*, vol. 32 (1987), pp. 123-128.Nieman, et al., "Clinical Applications of the Glucocorticoid and Progestin Antagonist RU 486," appearing in *Receptor Mediated Antisteroid Action*/Editor M. K. Agarwal (1987).

(List continue on next page.)

Primary Examiner—Raymond Henley, III*Attorney, Agent, or Firm*—Panitch Schwarze Jacobs & Nadel

[57]

ABSTRACT

Progression of chronic renal failure can be retarded or arrested by administering to humans suffering from such disorder an agent which suppresses the production of glucocorticoids in the human together with a glucocorticoid. An example of an agent which suppresses the production of glucocorticoids includes ketoconazole. Exemplary of the glucocorticoid is prednisone.

16 Claims, 1 Drawing Sheet